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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|-------------------|
| 09/852,922 | 05/10/2001 | Toshihiro Kuroita | 10089/14 | 5846 |
| 26646 | 7590 | 11/12/2004 | EXAMINER | |
| KENYON & KENYON ONE BROADWAY NEW YORK, NY 10004 | | | | HUTSON, RICHARD G |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1652 | |

DATE MAILED: 11/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 09/852,922 | KUROITA ET AL. | |
| | Examiner | Art Unit | |
| | Richard G. Hutson | 1652 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 08 September 2004.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-13,25-28 and 30-41 is/are pending in the application.
- 4a) Of the above claim(s) 13 and 31 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-3,25-28,30 and 32-41 is/are rejected.
- 7) Claim(s) 4-12 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All
 - b) Some *
 - c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/8/2004 has been entered.

Applicants amendment of claims 4, 5, 32, 35-38 and the addition of new claims 39-41, in the paper of 6/29/2004, is acknowledged. Claims 1-13, 25-28 and 30-41 are still at issue and are present for examination.

Election/Restrictions

Applicants comments regarding the patentable distinctness of claim 31 from the invention of claims 11-13, 25-28, 30 and 32-38 are acknowledged. Applicants continue to argue that claim 31 is drawn to a method of improving amplification efficiency and/or fidelity of a thermostable DNA polymerase and question how chemical synthesis can improve the amplification and/or fidelity if the main thing involved is an enzyme. Applicants thus request that claim 31 be rejoined with the other examined claims because the above and previously stated reasons for restriction are not supported by scientific reasoning.

Applicants traversal is acknowledged however not found persuasive on the basis that previously stated:

The invention of newly added claim 31 and Group I, currently being prosecuted, are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product can be made by a materially different process such as chemical synthesis. Applicants point that the invention of claim 31 is drawn to a method of improving amplification efficiency and/or fidelity of a thermostable DNA polymerase is appreciated, however this claim may also be considered a process of making the "improved thermostable DNA polymerase". This same "improved thermostable DNA polymerase" could be made from "scratch" (i.e. methods which do not comprise the modification of a naturally occurring thermostable polymerase) using common laboratory chemical synthesis methods in which the "improved thermostable DNA polymerase" was made by the addition of amino acid after amino acid etc...

Claims 13 and 31 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Objections

Claims 4-12 are objected to because of the following informalities:

Claims 4-12 are dependent on rejected claim 3.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Newly added claims 39-41 each recite the limitation "...having improved PCT amplification efficiency..." This recitation is indefinite in that it is unclear. For the purpose of advancing prosecution the recitation is interpreted as "...having improved PCR amplification efficiency..."

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 25-28, 30 and 32-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 1-12, 25-28, 30 and 32-38. In response to this rejection applicants have amended claims 4, 5, 32, 35-38 and added new claims 39-41 and traverse the rejection as it applies to these newly amended claims. Claims 39-41 are included in this rejection for the same reasons previously stated for claims 1-3, 25-28 and 30.

Applicants traverse this rejection on the basis that the specification provides sufficient written description because the specification describes a modified thermostable DNA polymerase comprising a $DX_1EX_2X_3X_4H$ sequence within the exonuclease I region of the thermostable DNA polymerase wherein histidine (H) has been replaced by another amino acid, wherein the modified thermostable DNA polymerase has modified 3'-5' exonuclease activity and/or amplification efficiency.

Applicants further point out their specification describes the structure to function /activity relationship in the disclosed species taught on page 20, line 19 to page 24 line 3 of the specification, which includes the effects of replacing histidine in the $DX_1EX_2X_3X_4H$ sequence with acidic, neutral or basic amino acids and the resulting effect.

Applicants argument is acknowledged, however found nonpersuasive because the above described structure to function/activity relationship is insufficient to describe the claimed genus of such modified DNA polymerases comprising any such modified DNA polymerase comprising the $DX_1EX_2X_3X_4H$ sequence.

Applicants attention is further directed to the currently rejected claims (i.e. claims 1-3) which are not limited to those modified DNA polymerases with the above discussed structure to function/activity relationship but rather applicants claims are limited to those modified DNA polymerases with the specified modification only. This includes both those that have the above described structure to function/activity relationship and those that have only a structural relationship.

Applicants argument is further found non-persuasive because applicants have not provided a sufficient number of representative species of polymerases prior to modification, having the DX₁EX₂X₃X₄H sequence encompassed by these claims. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-3, 25-28, 30 and 32-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a modified thermostable DNA polymerase having 3'-5' exonuclease activity, comprising SEQ ID NO: 2, wherein the histidine in the DIETLYH sequence at position 141 to 147 of SEQ ID NO: 2, has been replaced with another amino acid., does not reasonably provide enablement for

any modified thermostable DNA polymerase having 3'-5' exonuclease activity, wherein in the DX₁EX₂X₃X₄H sequence within the EXO I region of the thermostable DNA polymerase, histidine (H) has been replaced by another amino acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 1-12, 25-28 and 30. In response to this rejection applicants have amended claims 4, 5, 32, 35-38 and added new claims 39-41 and traverse the rejection as it applies to these newly amended claims. Claims 39-41 are included in this rejection for the same reasons previously stated for claims 1-12, 25-28 and 30.

Applicants traverse this rejection on the same basis as the above rejection based on a lack of written description, on the basis that applicants specification discloses the particular structure to function/activity relationship in various species of the modified thermostable DNA polymerase according to the claims (i.e. the effects of replacing histidine in the DX₁EX₂X₃X₄H sequence with acidic, neutral or basic amino acids and the resulting effect).

Applicants argument is acknowledged, however as above, found nonpersuasive because the above described structure to function/activity relationship is insufficient to fully enable the claimed genus of such modified DNA polymerases comprising any such modified DNA polymerase comprising the DX₁EX₂X₃X₄H sequence.

As above, applicants attention is further directed to the currently rejected claims (i.e. claims 1-3) which are not limited to those modified DNA polymerases with the above discussed structure to function/activity relationship, but rather applicants claims are limited to those modified DNA polymerases with the specified modification only. This includes both those that have the above described structure to function/activity relationship and those that have only a structural relationship.

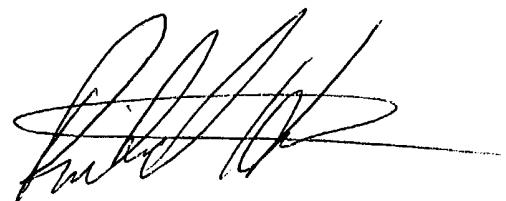
Applicants argument is further found non-persuasive because applicants have not provided a sufficient number of representative species of polymerases prior to modification, having the $DX_1EX_2X_3X_4H$ sequence encompassed by these claims. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to give sufficient guidance to fully enable the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any thermostable polymerase in the specified $DX_1EX_2X_3X_4H$ sequence. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rg
11/3/2004